

## Case Report

# Gastric aggressive fibromatosis: report of a case and review of the literature

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**Abstract:** Objectives: To describe a rare case of aggressive fibromatosis of the stomach and discuss the differential diagnoses. Methods: A 47-year-old man presented with nonspecific abdominal pain. Gastroscopy revealed stomach wall swelling. An antral gastrectomy was performed. Histological examination revealed spindle-shaped cells and morphology typical of aggressive fibromatosis. We performed a literature search to identify conditions with features similar to those of aggressive fibromatosis. Results: Aggressive fibromatosis does not metastasize, but it is locally invasive and has a tendency to relapse; however, our patient has not had recurrence > 1 year after surgery. Aggressive fibromatosis of the stomach may be confused with an inflammatory fibroid polyp, a gastrointestinal stromal tumor, schwannoma, leiomyoma, inflammatory myofibroblastic tumor, scirrhous carcinoma of the stomach, follicular dendritic cell sarcoma, inflammatory malignant fibrous histiocytoma, myofibroma/myofibromatosis, and solitary fibrous tumor of the stomach. Conclusions: Aggressive fibromatosis of the stomach is a rare spindle cell tumor that must be differentiated from a variety of conditions.

**Keywords:** Gastric tumor, aggressive fibromatosis, clinicopathological features, immunohistochemistry, differential diagnosis

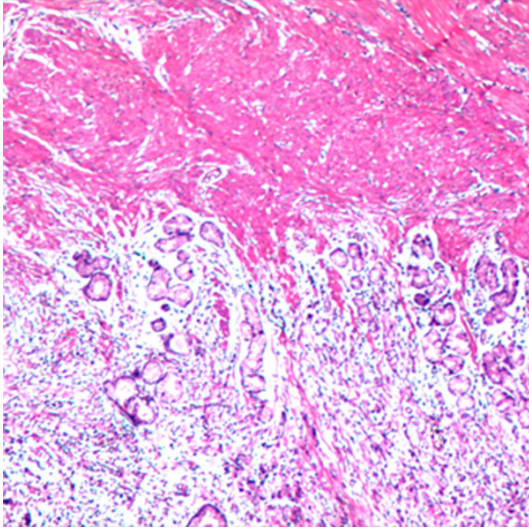
Aggressive fibromatosis is a fibrous tumor that most commonly occurs in the abdominal muscle layer and fascial sheath. It is also known as abdominal ligament-shaped fibroma, band-shaped tumor, desmoid tumor, fibrous tumor-like hyperplasia, abdominal recurrent fibrous-like tumor, and abdominal fibroma. Aggressive fibromatosis shows none of the characteristic signs of malignancy on cytological examination, nor does it metastasize; however, it is invasive and locally destructive, with a tendency to relapse after treatment [1]. According to the WHO (1994) definition, it is a differentiated fibroblastic tumor whose biological characteristics are intermediate between those of benign fibroblastic tumor and fibrous sarcoma [2].

In this paper we report a case of aggressive fibromatosis of the stomach and discuss the clinicopathological features, diagnosis, and differential diagnoses of this rare tumor.

### Case report

A 47-year-old man presented at the PLA 159th Hospital in Zhumadian, China, in August 2016 with complaints of abdominal pain and malaise. The pain was intermittent, continued until the patient's admission for surgery in September 2017, and was not accompanied by acid reflux, nausea, vomiting, diarrhea, or constipation. There were no other symptoms. He was a smoker (15 cigarettes per day for the past 35 years), and also had history of regular alcohol use (~50-150 mL per day). There was no family history of genetic disease. The physical examination was unremarkable. Gastroscopy revealed a swelling in the mucosa of the gastric antrum, so the patient was referred to the department of gastrointestinal surgery.

An antral gastrectomy was performed. An intra-operative frozen section examination revealed



**Figure 1.** Tumor tissue invasion of the mucous layer of the stomach. The intrinsic glands of the mucous layer show atrophy, hyperplasia, and atypia.

spindle-shaped cells and morphology suggestive of aggressive fibromatosis. The resection margins were free of tumor. On gross examination, the mass was 5.8 cm × 4.3 cm × 3.4 cm in size, hard in consistency, and gray-white in color, with ill-defined borders. There were no signs of hemorrhage, necrosis, or cystic degeneration.

The tumor was sectioned and stained with hematoxylin and eosin stain (HE) for histological examination. The EnVision™ (Dako, Carpinteria, CA, USA) staining method was used for immunohistochemical analysis. On microscopic examination, the tumor was located in the submucosa and showed invasive growth. Tumor tissue had invaded all three layers of the gastric wall. The overlying gastric mucosa showed areas of necrosis and ulceration. There was atrophy, hyperplasia, and heterology of the glands in the mucosa. The tumor tissue had pushed the smooth muscle tissue into the inherent layer (**Figure 1**). In the muscularis externa layer, tumor invasion separated the smooth muscle tissue into masses and nests of uneven sizes (**Figure 2**). In addition, the muscle was pushed away 10 mm from the tumor. There was thickening of the serosa because of the tumor invasion. The adipose tissue was separated into clumps by the ingrowth of tumor tissue (**Figure 3**). The normal morphology of blood vessels, lymphatic vessels and nerve tissue was destroyed, eliminating one of the important diagnostic points (**Figure 4**). The

tumor itself was composed of proliferative spindle-shaped fibroblasts of uniform morphology and collagen fibers. The appearance was consistent with fibroblastoma. The tumor cells contained abundant, lightly stained cytoplasm with an unclear cytoplasmic membrane (**Figure 5**). The nuclei were thin, fusiform or rod shaped, and had dark staining chromatin. There was no atypia, and mitotic figures were rare (0-3/50 HPF). Cell density was slightly higher near the gastric muscle layer than near the serosa. At times the collagenous fibers formed wide, long bands. No necrosis was found within the tumor. Tumor tissue also contained ganglion-like myofibroblasts, with vacuolated nuclei, eosinophilic nucleolus (or no) and abundant cytoplasmic inclusions and staining. There were scattered clusters of lymphocytes forming nodules in the tumor tissue, but these did not have a lymph node structure. In addition, small blood vessels and lymph nodules formed by neoplastic fibrous tissue were inside the lymphocytes. The clustered lymphocytes did not form germinal centers (**Figure 5**).

On immunohistochemical analysis, the tumor cells were positive for vimentin and  $\beta$ -catenin. SMA was positively expressed in some regions. Tumor cells were negative for CKpan, EMA, S-100 protein, desmin, CD99, Bcl-2, ALK, CD-34, CD68, CD163, CD21, CD23, CD117, DOG1, and hormone receptors. The Ki67 proliferation index was 0%-10% (**Figure 6**).

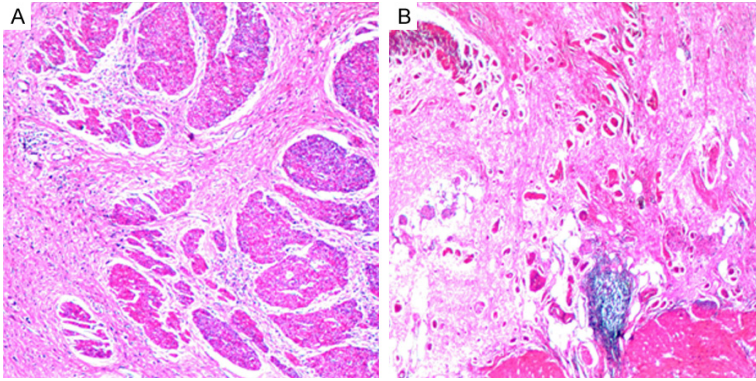
Postoperative recovery was uneventful. The patient was followed up regularly once a month. At the last follow-up (over the telephone), 13 months after surgery, he did not report any recurrence of the symptoms.

### Discussion

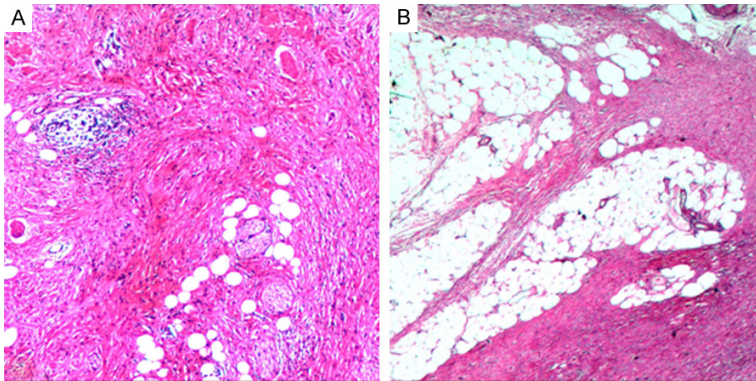
Aggressive fibromatosis is an abnormal hyperplasia of fibroblasts and/or myofibroblasts in deep soft tissue. It is characterized by invasive growth and a tendency for recurrence. According to the 2013 WHO classification, these tumors are categorized as intermediate (rarely metastasizing) locally invasive tumors. The etiology of the disease is not established. Injury, endocrine disorder, and chromosome abnormalities have been hypothesized as possible etiological factors [2]. It occurs most commonly between the ages of 10 and 40 years and affects both sexes equally. These tumors can be of three types according to the location:



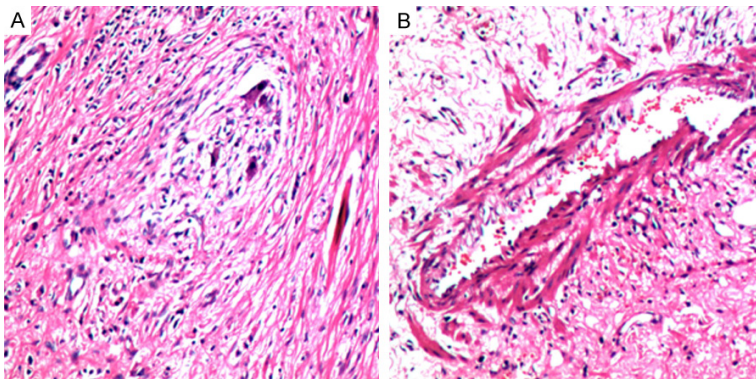
## Aggressive fibromatosis of the stomach



**Figure 2.** Tumor tissue invasion of the gastric muscle layer. A. The smooth muscle tissue is divided into masses and nests of uneven sizes; B. The invaded smooth muscle pieces were pushed to 10 mm away.



**Figure 3.** Tumor tissue invasion of the serous layer. A. The adipose tissue is separated into clumps; B. Tumor ingrowth into the adipose tissue.



**Figure 4.** Invasion by tumor tissue has destroyed the morphology of blood vessels and nerve tissue. A. Only incomplete ganglion cells are seen as a result of tumor invasion of nerve tissue. B. Tumor invasion has destroyed blood vessels.

abdominal fibroma, fibroma outside the abdominal wall, fibroma of abdominal cavity and mesentery. A ligament-like fibroma occurring at sites other than the abdominal wall mainly

involves the skeletal muscle of the neck, shoulder, limbs, and sometimes the intracranium, thorax, mammary gland, and thyroid [2-5].

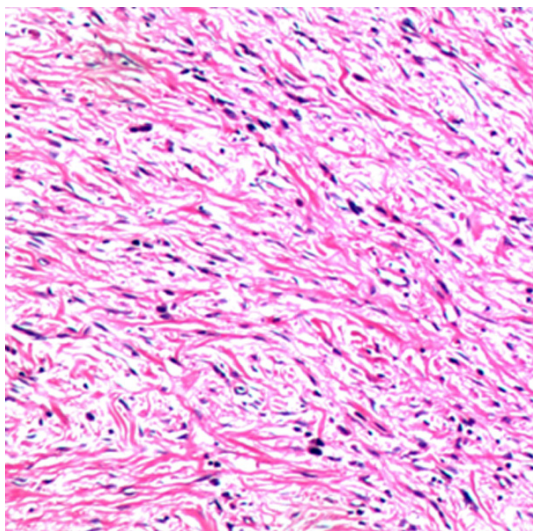
Aggressive fibromatosis of the stomach is rare. The clinical manifestations are nonspecific, with patients mostly complaining of abdominal pain and distension; a mass may sometimes be palpable. Invasion of the gastric mucosa may lead to ulcers and gastric bleeding and even hematemesis. The most important means of clinical examination is gastroscopy.

Differential diagnoses include inflammatory fibroid polyp, gastrointestinal stromal tumor (GIST), schwannoma, leiomyoma, inflammatory myofibroblastic tumor, scirrhous carcinoma of the stomach, follicular dendritic cell sarcoma, inflammatory malignant fibrous histiocytoma, myofibroma/myofibromatosis, and solitary fibrous tumor of stomach.

An inflammatory fibroid polyp usually occurs in older patients (60-75 years old). It manifests as a sessile, polyp-like swelling of about 1.5 cm in diameter. It is composed of loose connective tissue, spindle-shaped fibroblasts, inflammatory cells (mainly lymphocytes and eosinophilic granulocytes), and thin-walled blood vessels and local edema or a mucosal background. It is positive for vimentin and CD-34 but negative for ALK and  $\beta$ -catenin. SMA may be expressed in some regions [6, 7].

A gastrointestinal stromal tumor (GIST) is the most common mesenchymal tumor. It is composed of dense collections of fusiform, round, or epithelioid cells and shows different degrees

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**Figure 5.** The tumor is composed of uniform proliferative spindle-shaped fibroblasts and collagen fibers. Tumor tissue is mostly arranged in the form of staggered bundles.

of atypia. Mitotic figures are common. It is positive for CD117 and GOG1, and sometimes for CD34, SMA, and S-100 protein. *KIT* or *PDGFRA* gene mutations are present [8, 9].

Schwannoma of the stomach mostly occurs in the elderly, manifesting as a 2-5 cm swelling in the wall of the stomach. The clinical manifestations are similar to those of GIST. It shows benign behavior, and recurrence is rare. The tumor is composed of spindle cells, arranged in crisscrossing bundles. The nuclei show a “picket fence” arrangement. Variable amounts of collagen fiber are present between the cells. The tumor is surrounded by nodular nests of lymphocytes. Tumor cells express S-100 protein, Leu-7, PGP9.5, and GFAP, and other nerve markers. Some tumors also express CD34. Tumor cells are negative for CD117, DOG1, ALK, desmin, and SMA [6, 10, 11].

Leiomyoma of the digestive tract is more common in the esophagus and colon than in the stomach. Tumors may range in size from tiny nodules to masses with a diameter > 5 cm. It is composed of well-differentiated smooth muscle cells, with little or no atypia. The tumor is positive for desmin and SMA, but negative for CD117, ALK, and CD34 [2].

Inflammatory myofibroblastic tumor mainly occurs in children < 10 years old. It is com-

posed of proliferative hypertrophic spindle-shaped fibroblasts or myofibroblasts. Heavy inflammatory cell infiltration is present, mostly with mature plasma cells, lymphocytes, and eosinophilic granulocytes. Round histiocyte-like cells may be present. In some cases, irregular, polygonal or bizarre-shaped cells may be observed, with eosinophilic or basophilic inclusions in the nuclei, presenting a picture similar to that of ganglion cells or Reed-Sternberg cells. The tumor is positive for vimentin and SMA. Desmin may be positively expressed in some areas. About half of the cases express ALK. The tumor cells are negative for CD117, DOG1,  $\beta$ -catenin, and S-100 protein [12, 13].

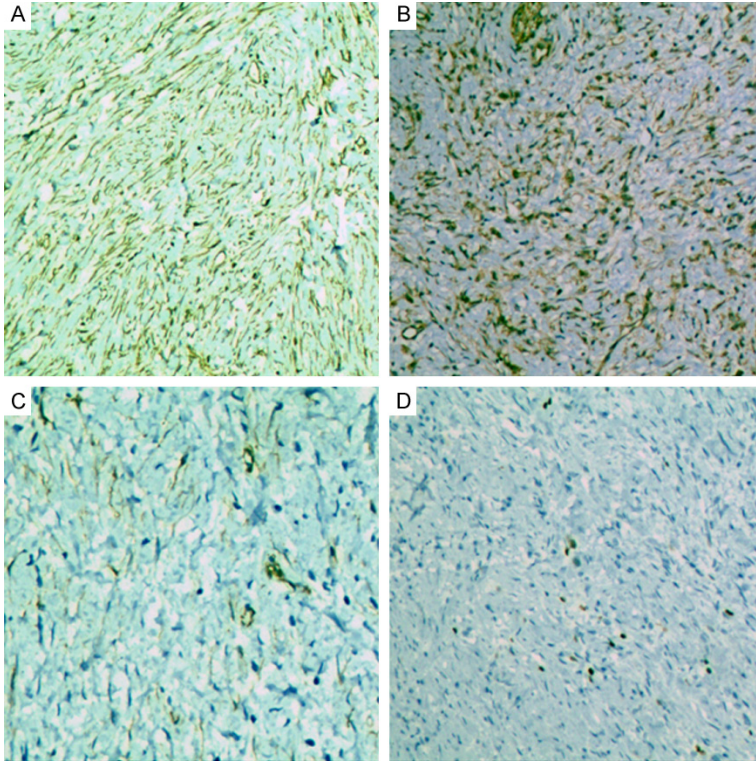
Scirrhus carcinoma of stomach is most often seen in the 30-40 year age-group. Clinical manifestations include anorexia and emaciation. The tumor cells are small and scattered or are clustered between fibrous connective tissue. Sometimes the tumor may contain spindle-shaped or irregular-shaped cells. Glandular structure is lost. Mitotic figures are common (1-5/1 HPF). The tumor shows invasive growth, and lymphatic and vascular metastasis can occur. Prognosis is poor. The tumor is positive for CKpan, CK8/18, CK19, CK20, EMA, and CEA, and negative for vimentin, SMA, desmin, and S-100 protein. Ki-67-positive cell number is 70%-80% [14-18].

Follicular dendritic cell sarcoma mostly occurs in lymph nodes. Other sites include tonsils, the oral cavity, soft tissue, skin, gastrointestinal tract, mediastinum, liver, and spleen. The tumor cells are fusiform, with vacuolated nuclei and distinct nucleoli. Multicellular cells or conjugate cells, similar to Warthin-Finkeldey giant cells, may be present. Mitotic figures may be seen (0-10/10 HPF). Necrotic areas are common. Histologically, the proliferative fusiform and oval cells form a drawstring bundle, vortex, and textured arrangement. They may form lymphatic sleeves around vessels. Dilated cystic cavities containing light red protein liquid may be present. Tumor cells are positive for clusterin, CD19, CD21, CD23, CD35, R4/23, Ki-M4, Ki-M4p, desmoplakin, and vimentin, but negative for SMA [2, 6].

Inflammatory malignant fibrous histiocytoma is usually seen in patients > 40 years old and is most commonly retroperitoneal in location. Yellow tumor cells and pleomorphic cells similar



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**Figure 6.** Immunophenotyping of gastric fibromatosis (EnVision method). A. Positive expression of vimentin; B. Positive expression of  $\beta$ -catenin; C. Positive expression of SMA in partial lesion. D. The ki-67-positive cell number is 0%-10%.

to Reed-Sternberg cells are seen on microscopic examination. Large numbers of neutrophils, eosinophilic granulocytes, and a few lymphatic plasma cells may be seen. Atypia is more common than in inflammatory myofibroblastic tumor. The tumor is positive for CD68, lysozyme, and vimentin, but negative for SMA, desmin, and CK [2, 6].

Myofibroma/myofibromatosis is a benign tumor with contractile muscle-like cells arranged around thin-walled blood vessels. The tumor can occur in patients of any age but is most commonly seen in infants < 2 years old. It is more common in males. It mainly occurs in the head and neck, torso, and limb. Only about 15%-20% occur in the viscera. The tumor cell is spindle-shaped and contains light pink-stained cytoplasm and an elongated, spindle-shaped, vacuolated nucleus with 1-2 small nucleoli. Cellular atypia and polymorphism are not obvious. The tumor cells are arranged around peripheral thin-walled vessels with irregular branches, intersected with the vascular periph-

eral mycetoma. The histological picture is similar to that of hemangioma. Calcification, glass-like degeneration, necrosis, and apoptosis are common. Usually, there is no marked infiltration by lymphocytes and plasma cells. The tumor is positive for vimentin and SMA. Total actin HHF35 is positively expressed in a stronger signal. It is negative for CK, EMA, and S-100 [2, 6].

Solitary fibrous tumor of the stomach is made up of irregularly distributed tumor cell-sparse and tumor cell-rich regions, with interspersed dense collagen fiber deposition and hemangioma-like regions. Moderate to severe atypia is present and there may be areas of necrosis. Lymph node metastasis is possible. The tumor is positive for CD99, CD34, Bcl-2, and vimentin. CKpan, EMA, SMA, S-100 protein, and desmin may be weakly positive in parts of the

lesion. It is negative for ALK, CD68, CD163, CD21, CD23,  $\beta$ -catenin, and CD117, DOG1 [19, 20].

In conclusion, aggressive fibromatosis is a rare tumor that shows locally invasive behavior. Surgical resection is the main method of treatment. The disease has a very high recurrence rate, so close follow-up is necessary after surgery.

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### Disclosure of conflict of interest

None.

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